Chaetomellic Acid A treatment improves oxidative stress in rats with renal mass reduction

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Chaetomellic acid A (CA) is a potent and highly specific inhibitor of Ras farnesyl-protein transferase that has shown to decrease oxidative stress in rats with brain damage. Oxidative stress has been suggested to play an important role in the pathogenesis of chronic renal disease. Thus, the aim of this work was to evaluate the effect of chronic treatment with CA on oxidative stress in a model of renal mass reduction. Male Wistar rats were subjected to 5/6 nephrectomy (RMR) or sham-operated (SO). One week after surgery, rats have been placed in four experimental groups: RMR rats without treatment (n=12); RMR rats treated with CA (n=8); SO rats without treatment (n=13); SO rats treated with CA (n=13). CA was intraperitoneally administered in a dose of 0.23 µg/Kg three times a week for six months. To evaluate the effect of CA on renal redox potential, the status of oxidative stress in renal tissues was determined. RMR was accompanied by a significant reduction in catalase and glutathione reductase (GR) activity, and a decrease in reduced glutathione (GSH)/oxidized glutathione (GSSG) ratio. CA administration significantly increased catalase and GR activity (p<0.05), and increased GSH/GSSG ratio, but no significant difference between the treated and no treated groups was found in this ratio. These data suggest that CA can attenuate 5/6 RMR-induced oxidative stress and therefore, contribute to prevention of progressive renal failure in chronic renal disease.